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Eur J Immunol. 2003 Jul;33(7):1998-2006.

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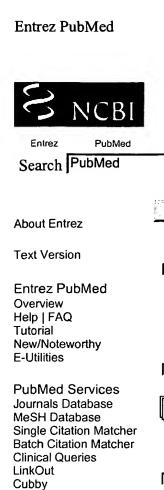
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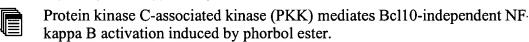
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Activation of NF-kappaB by FADD, Casper, and caspase-8.

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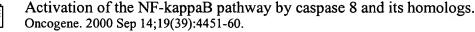


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	Mouse receptor interacting protein 3 does not contain a caspa death domain but induces apoptosis and activates NF-kappaE Mol Cell Biol. 1999 Oct;19(10):6500-8. PMID: 10490590 [PubMed - indexed for MEDLINE]	_
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- Caspase-8 and caspase-10 activate NF-kappaB through RIP, NIK and IKKalpha TIkinases.
- AU Shikama Yoshiaki; Yamada Masao; Miyashita Toshiyuki
- CS Department of Genetics, National Research Institute for Child Health and Development, 3-35-31 Taishido, Setagaya-ku, Tokyo 154-8567, Japan.
- SO European journal of immunology, (2003 Jul) 33 (7) 1998-2006. Journal code: 1273201. ISSN: 0014-2980.
- CY Germany: Germany, Federal Republic of
- DT Journal; Article; (JOURNAL ARTICLE)
- LΆ English
- FS Priority Journals
- EM 200308
- ED Entered STN: 20030730 Last Updated on STN: 20030828 Entered Medline: 20030827
- AB NF-kappaB regulates the expression of various genes involved in cell growth and differentiation, immune response and inhibition of apoptosis. Recently, some death effector domain (DED)-containing proteins, such as FADD and c-FLIP were reported to activate NF-kappaB. We previously reported that the prodomain-only isoforms of caspase-8 and -10 (PDCasp8/10), containing two DED motifs, could inhibit Fas-mediated apoptosis. Here, we demonstrate that these isoforms also activate NF-kappaB, implying this to be one of the mechanisms by which these polypeptides inhibit apoptosis. The GST pull-down assay revealed that, among upstream kinases that activate NF-kappaB, only NIK and RIP, but not RICK or IKKalpha/beta, could directly bind to PDCasp8/10. In addition, both modules of DED in PDCasp8/10 were required for these interactions as

well as NF-kappaB activation. Experiments using a kinase-dead mutant of IKKalpha and an RIP mutant lacking a kinase domain, both of which function as dominant-negative mutants for their wild-type counterparts, blocked PDCasp8/10-mediated NF-kappaB activation. Using small interfering RNA technology, we further demonstrate that the down-regulation of IKKalpha but not IKKbeta significantly inhibits PDCasp8-mediated NF-kappaB activation. Taken together, these results suggest that caspase-8 and -10 have roles in a non- or anti-apoptotic signaling pathway leading to NF-kappaB activation through RIP, NIK and IKKalpha.

- L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
- AN 2002:616256 CAPLUS
- DN 137:181594
- TI Dominant-negative variants of human protein kinases that inhibit the phosphorylation activity of their active enzyme isoforms
- IN Levine, Zurit; Bernstein, Jeanne
- PA Compugen Ltd., Israel
- SO U.S. Pat. Appl. Publ., 170 pp., Cont.-in-part of U.S. Ser. No. 724,676. CODEN: USXXCO
- DT Patent
- LA English
- FAN.CNT 1

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PRAI	IL 2000-135619	Α	20000512		
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	US 2000-724676	A2	20001128		

AB The present invention concerns 91 nucleic acid sequences and amino acid sequences of variants of various human kinases, i.e. of sequences which inhibit activity of kinases in a dominant manner. The variants lack a domain or region required for phosphorylation, and thus may be dominant-neg. kinases obtained by alternative splicing of known original sequences of the kinase genes. The novel dominant-neg. kinase variants of the invention are not merely artificially truncated forms, fragments or mutations of known genes, but rather novel sequences which naturally occur within the body of individuals. The invention also concerns pharmaceutical compns. and detection methods using these sequences.

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